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ABSTRACT

Examined were medical records of 265 hyperkinetic children (7-9 years old). Clinical blood chemistries, hematology, and 5-hour glucose tolerance test (GTT) results indicated that hematocrit levels were low in 27% of the Ss, eosinophil levels were abnormally high in 86% of the Ss, and GTT results were abnormal in a majority of Ss. (CL)

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GLUCOSE TOLERANCE AND HYPERKINESIS

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Abstract - The medical records of 265 carefully selected hyperkinetic children were studied. The children had been admitted on an out-patient basis to a treatment center during the period 1973 to 1976. All the children had been previously diagnosed as hyperkinetic at least once by a physician and up to three additional times by parents, teachers, or physicians. Adopted children and children with other known physicial or emotional disturbances were excluded from the study.

Medical records were studied for clinical blood chemistries, hematology, and five hour glucose tolerance test results. Of the total 16 parameters studied 13 did not reveal significant deviations from normal values. However, hematocrit levels were low in 27% of the cases, eosinophil levels were abnormally high in 86% and in a majority of cases GTT results were abnormal.

Of the abnormal GTT curves 50% were characterized by low, flat curves. The second most prominent type of abnormal GTT (27%) was characterized by excessive peaks and slow recovery. In about half of these cases there were elevated cholesterol levels and glucose in the urine. The other abnormal curves were characterized by excessive peaks with rapid declines or flat curves with terminal values higher than any other values in the curve.

It appears that a majority of the children have abnormal patterns of glucose metabolism. Additional studies should be conducted to investigate this phenomenon as one possible factor in the etiology of hyperkinesis.

INTRODUCTION

Hyperkinesis has received much attention over the past decade and is being diagnosed with increasing frequency. The term "hyperkinesis" refers to a broad range of behavioral systems seen in children, but not found in adults. The syndrome is characterized by inappropriate and excessive physical activity, a short attention span, and a hyper-response to environmental stimuli (Holvey, 1972). It has been assoicated with trauma at birth, (Hoffman, 1971; Towbin, 1971), excessive body burdens of lead (David, 1974) emotional stress (Wender, 1971), and diet (Feingold, 1976). In the latter case hyperkinesis has been claimed to be specifically associated with food colors and food "additives." However, no conclusive evidence exists that bears out a strong cause and effect relationship between the ingestion of food colors or other additives and hyperkinesis (Kolbye, 1976; Lipton, 1975). A review of the literature did not reveal any studies of hyperkinesis based on clinical chemistries of those affected with the syndrome. Here we report a clinical study of 265 carefully screened children diagnosed as hyperkinetic.

EXPERIMENTAL

PATIENTS AND METHODS

The data used in this study was obtained from medical records of 265 hyperkinetic children, admitted on an out-patient basis, to the The New York Institute for Child Development between 1973 and 1976. Each child had been diagnosed as hyperkinetic at least once by a parent, teacher, or a physician. In addition, before being admitted to the Institute for treatment, the diagnosis of hyperkinesis was confirmed by one of the physicians at the Institute. Hyperkinetic children with other known emotional or motor disturbances were excluded from the study.

Records of the 265 children in the seven to nine year age range were studied. Age nine was used as the upper cut-off point in order to avoid the onset of puberty as another variable in the study. Adopted children were not used in the study becuase of the difficulty in obtaining family histories. No attempt was made to select any particular sex or ethnic ratio among the children studied.

Two hundred forty-nine children in the study were Causcasian, nine were Black, and seven were Hispanic. This is not necessarily an indication that hyperkinesis is more prevalent among whites than among other ethnic groups, but rather representative of a socio-enonomic phenomenon. The socio-economic level of the children was predominatly middle strata.

At the Institute each child was evaluated by a physical therapist, a nutritionist and a physician. The patient's dietary and drug history was recorded as well as his medical history, which included any incidence of colic, allergies, anemia, gastrointestinal problems, thyroid dysfunction,

diabetes, and low blood sugar. The medical history of the patient's family was also recorded as best it could be ascertained.

Blood chemistries of serum samples from the children were analyzed for the following parameters: bilirubin, blood urea nitrogen (BUN), calcium, cholesterol, protein bound iodine (PBI), phosphorus, total protein, SGOT (serum glutamic oxalacetic transaminase), SPGT (serum glutamic pyruvic transaminase), and uric acid. Five-hour oral glucose tolerance test (GTT) results were also studied, and urine samples, taken at the same intervals as GTT blood samples, were analyzed in order to determine if there was any glucose or acetone present in the urine.

The information on each subject was analyzed by computer to examine distributions, trends and correlations. The normal values for each parameter of clinical chemistry studied were based on those in Todd and Sanford (1969) and the Merck Manual (Holvey, 1972). The widest possible range of normal values were used. In the case of the GTT median values were used and then a $\pm$ 20 point spread was added to denote the "normal range."

RESULTS

There were no strong correlations or patterns evident in family or patient history. There were a number of subjects and their families with histories of allergies, diabetes, and anemia, however, these were not found to be different from the incidence found in a normal population.

A summary of the clinical blood chemistries is presented in Table 1. Of the 10 parameters of blood chemistry analyzed, none showed significant deviations from the norm.

Results of the hematology studies, presented in Table 2, show that values were outside the normal range for two parameters investigated: hematocrit and eosinophil counts. The greatest number of cases deviating from the norm occured in eosinophil counts, with 86% of the subjects exhibiting higher values than normal.

Table 3 shows a summary of the (GTT) results after each interval that blood samples were drawn. Lower than normal values predominated, although there were some individuals who showed a greater than normal response. The highest percentage of abnormalties (88%) appeared one hour after administration of glucose.

The (GTT) test data was also studied in terms of the response curve as a whole. There was sufficient data to do this in 261 cases. Twenty-six percent of the curves appeared to be normal, while 74% showed abnormalties. Figure 1 shows a normal (GTT) curve. The most frequently observed abnormal curves are illustrated in Figures 2 - 5.

The predominant abnormality, accounting for 50% of the abnormal (GTT) results, was a low flat curve (Figure 2). Fifteen percent of the curves evidenced abnormally high peaks with extremely rapid declines (Figure 3), and almost 11%, or 21 cases, had abnormally high peaks with slow recovery times (Figure 4). In 15 of the 21 subjects with this latter type of curve elevated cholesterol levels were also found. Glucose was present in urine during peak

serum glucose levels in 13/21 of these cases. Almost 11% of the abnormal curves showed a decline immediately after glucose ingestion with a slow rise in glucose levels and a terminal value higher than fasting values (Figure 5). Of the remaining 14% of the abnormal curves 8% were characterized by normal peaks with slow declines and 6% with high late peaks or rapid declines.

DISCUSSION

Of the 265 children in the study, 211 were males, and 54 were females. The predominance of males to females is a well-known phenomenon when dealing with hyperkinesis (Kolbye, 1976). The ratio in this study was about 4:1 male to female. However, it should be remembered that an effort was made to screen out subjects with problems other than hyperkinesis. It is also interesting to note that a 4:1 male to female ratio is consistent with the expected distribution for an x-linked recessive trait (McKusick, 1964).

From an analysis of the clinical data two distinct abnormalities were seen: raised eosinophil counts, and abnormal glucose tolerance test results.

Elevated eosinophil counts may be a reflection of the incidence of known allergies in the subjects. However, this explanation does not account for elevated levels in all cases, since 45% of those with elevated counts did not report any known allergies. Also, since the test subjects were admitted to the Institute and tested throughout the year, high pollen counts during summer months cannot be blamed for the elevated eosinophil levels. Drug therapy can also cause eosinophilia, however, only 20% of the children were receiving drug therapy at the time of admission. No explanation of this phenomenon is offered, although it is possible that eosinophil counts could be used as indicators to monitor the progress of a particular treatment for hyperkinesis.

The GTT data clearly indicate that a large number of the hyperkinetic children tested have abnormal patterns of glucose metabolism. There were four types of abnormal GTT curves found in a significant percentage of children.

The low, flat curve shown in Figure 2 (50% of the abnormal cases) is

similar to that seen in hypoglycemics. Hypoglycemia is a potent stimulus for increased production of epinephrine (Ganong, 1975), and characteristic neverousness or hyperkinetic behavior observed in these children is not unlike that seen in hypoglycemics. It appears that many of these children may indeed be undiagnosed hypoglycemics.

The second type of abnormal curve of particular interest is distinguished by excessively high peaks and slow recovery times (11% of the abnormal curves) as shown in Figure 3. These curves are similar to those found in pre-diabetic children. In the majority of cases these curves were associated with glucose in the urine and elevated cholesterol levels, both signs common in diabetes. The curves with abnormally high peaks and rapid declines (shown in Figure 4) may also be related to early diabetes. However, the relationship here is not as clear as with the curves with abnormally high peaks and slow declines.

It is interesting to note here that many hyperkinetic children have slow growth rates. This has been attributed to Ritalin, the drug of choice for hyperkinetics (Huff, 1975). However, children with diabetes also do not thrive and the slower growth rates in hyperkinetic children could be related to the possibility mentioned above, that some of them are early diabetics.

Some of the GTT curves with elevated peaks and slow recovery times might also be interpreted as being due to liver damage from drug therapy. Forty-one percent of the subjects had been on drug therapy prior to admission and twenty percent of the children were receiving drugs at the time of admission.

The type GTT response which we have named "half moon," (shown in Figure 5)

may be the result of an overproduction of insulin which could rapidly lower the glucose level in the blood serum immediately following the ingestion of glucose. This type of response is sometimes observed in certain types of hypoglycemics.

We studied the distribution of abnormal GTT results relative to drug therapy and found no strong correlations. There were abnormal curves for children on or off drugs. Conversely, there were normal curves found in children in both categories.

Hoffman (1971) has associated hyperkinetic syndrome with trauma at birth, low birth weight, poor nutrition, and brain damage. In a number of instances where this investigator conducted GTT on subjects, she reported low, flat GTT curves, very much like the ones found in this study.

Crook (1976) has studied food allergy as it relates to hyperkinetic behavior. He began working with food colors and additives but later found that other foods were suspected of illiciting hyperkinetic behavior. He recently reported that sugar was probably the second most frequent dietary cause of hyperkinetic behavior in susceptible children. Similar findings were reported by Rapp (1976) who found that children challenged with sugar alone showed hyperkinetic responses nearly as great as children challenged with sugar and food dye.

Based on results of the GTT a diet program at the Institute was initiated. The Institute now routinely prescribes a diet high in protein, and low in carbohyrdates, especially sugars. The diet program appears to have had positive results in reducing and in some cases eliminating hyperkinetic behavior. Recurrences of hyperkinetic behavior have in a large number of cases been associated with, among other factors, the ingestion of large amounts of sugar.

Based on the results of this study there are several models that can be constructed to explain the hyperkinesis phenomenon. The most obvious one involves adrenergic response (Schildkrut, 1976; Howell, 1972). A diet high in refined carbohydrates stimulates insulin production which in turn stimulates an adrenergic response. Ultimately the adrenergic response triggers production of epinephrine/nonepinephrine. High levels of these hormones can cause the type of behavior seen in hyperkinetic children.

The authors are aware of the short commings of the glucose tolerance test. However, even with these considerations, it appears that there are sufficient deviations from generally accepted norms to indicate that glucose metabolism in hyperkinetic children is an area that should be further investigated. There are no doubt many etiologies for this disorder. This study suggests one possible dietary contributing or causative factor.

Acknowledgements

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REFERENCES

Crook, W.G. (1976). Learning Disabilities & Hyperactivity in Children Due to Foods. Presented at the International Food Allergy Symposium, Toronto, Canada.

David, O.J. (1974). Environ. Health Perspect. May, 17.

Feingold, B.F.J. (1976). Journal of Learning Disabilities 9, 19.

Ganong, W.F. (1976). Review of Medical Physiology - 7th Ed., Lange Medical Publications, Los Altos, California.

Hoffman, M.S. (1971). The Nutritional Aspects of Learning Disabilities. Presented at the 7th Annual Convention of the Texas Association for Children with Learning Disabilities, Dallas, Texas.

Howell, M.C., Rever, G.W., School, M.L. (1972). Clin. Pediatr. 11, 1.

Kolbye, A.C. (1976). First Report of the Preliminary Findings & Recommendations of the Interagency Collaborative Group on Hyperkinesis. Bureau of Foods, Food and Drug Administration.

McKusick, V.A. (1964). Human Genetics. Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

Holvey, D.N. (1972). Merck Manual - 12th Ed., Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey.

Lipton, M. (1975). National Advisory Committee on Hyperkinesis & Food Additives - Report to the Nutrition Foundation. University of North Carolina, Chapel Hill, North Carolina.

Huff, B.B. (1975). Physicians' Desk Reference - 29th Ed., Medical Economics Co., Oradell, New Jersey.

Rapp, D.J. (1976). Double Blind Study in Relation to the Role of Foods & Dyes to Hyperactivity. Presented at the International Food Allergy Symposium, Toronto, Canada.

Schildkraut, J.J., Kety, S.S. (1976). Science. 156, 3771.

Todd & Sanford (1969). Clinical Diagnosis by Laboratory Methods - 14th Ed., W.B. Saunders Co., Philadelphia, Pennsylvania.

Towbin, A. (1971). JAMA. 217, 9.

Wender, P. (1971). Minimal Brain Dysfunction in Children. Willy & Sons, New York, New York.

Table 1. *Results of Blood Chemistry Analyses*

Test/Units	Name of Test	Range of Normal Values		Number of Subjects Tested	Number of Test Subjects with Test Values Outside Normal Range		Total Percent Abnormal Value in Subjects Tested
		Low	High		Low	High	
Bilirubin mg %	Bilirubin	0.15	1.05	239	7	6	5.00
BUN mg%	BUN	8.50	20.00	244	1	7	3.00
Calcium mg %	Calcium	8.50	11.20	253	8	3	3.50
Cholesterol Ug %	Cholesterol	120.00	230.00	245	4	15	7.00
PBI mg %	PBI	3.50	8.80	95	0	7	7.00
Phosphorus	Phosphorus	2.00	7.00	235	1	0	0.40
Protein g %	Protein	5.90	8.00	251	1	11	4.70
(total)	SGOT	20.00	80.00	240	25	2	11.25
SGOT mU/ml	SGPT	5.00	35.00	73	5	8	17.80
SGPT IU/ml	Uric Acid	2.00	8.50	247	0	2	1.00
Uric Acid mg %							

BUN = Blood urea nitrogen

PBI = Protein bound iodine

SGOT = Serum Glutamic Oxalacetic Transaminase

SGPT = Serum Glutamic Pyruvic Transaminase

Table 2. *Summary of Hematology Test Data*

Name of Test	Range of Normal Values Low	High	Number of Subjects Tested	Number of Test Subjects with Test Values Outside Normal Range Low	High	Total Percent Abnormal Values in Tested Subjects
Hemoglobin gm%	12.00	18.00	261	25	0	9.5
Hematocrit ml %	37.00	52.00	247	68	0	27.5
WBC	5.00	10.00	260	34	10	16.9
RBC	4.20	6.20	207	25	1	12.5
Eosinophils %	0.00	0.06	245	0	211	86.0

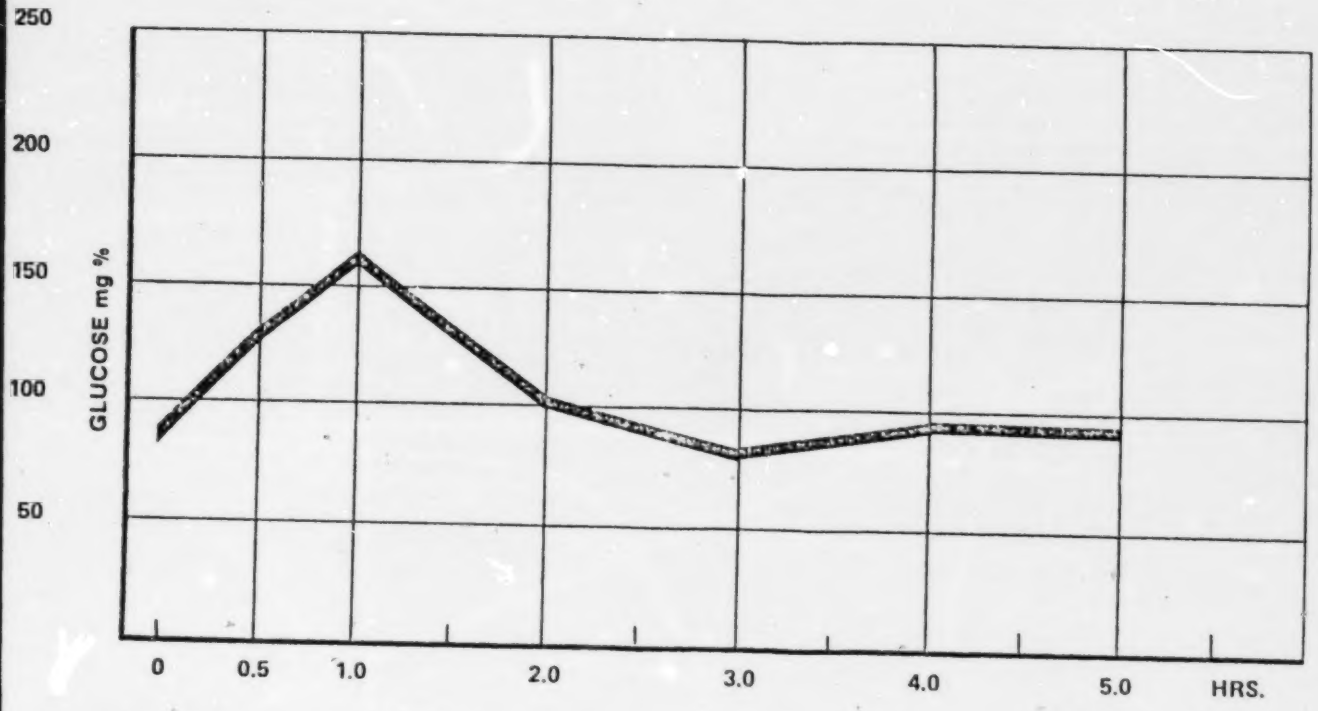
WBC = White Blood Count x 10^{3} cells/mm^{3}

RBC = Red Blood Count x 10^{6} cells/mm^{3}

Table 3. *Summary of Glucose Tolerance Test (GTT)*

Time Blood Serum was Drawn	Range of Normal Values* Low	High	Number of Subects Tested	Number of Test Subjects with Test Results Outside of Normal Range Low	High	Total % Abnormal Values in Subjects Tested
0 (Fasting)	65.00	105.00	265	8	25	12.0
30 Minutes	105.00	145.00	194	47	65	57.0
1 Hour	140.00	180.00	281	221	9	88.0
2 Hours	80.00	120.00	262	50	37	30.0
3 Hours	60.00	100.00	258	14	58	28.0
4 Hours	70.00	110.00	247	29	16	18.0
5 Hours	68.00	108.00	239	14	16	12.5

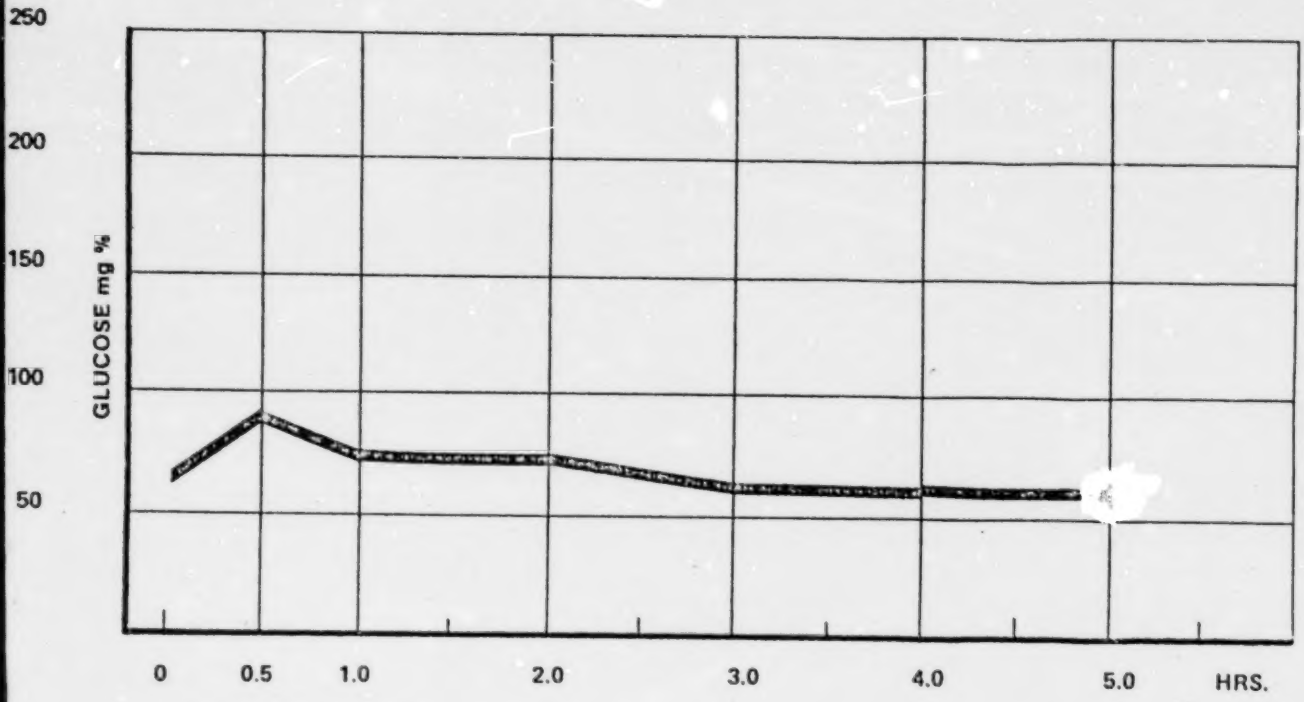
*mg%



RISE TIME 0.50 HRS.
PEAK VALUE 147
GRADIENT FROM PEAK TO 3 HOURS – 23.6
GRADIENT FROM PEAK TO 4 HOURS – 15.7
GRADIENT FROM PEAK TO 5 HOURS – 11.1

Fig. 1. Normal Glucose Tolerance Test Curve.

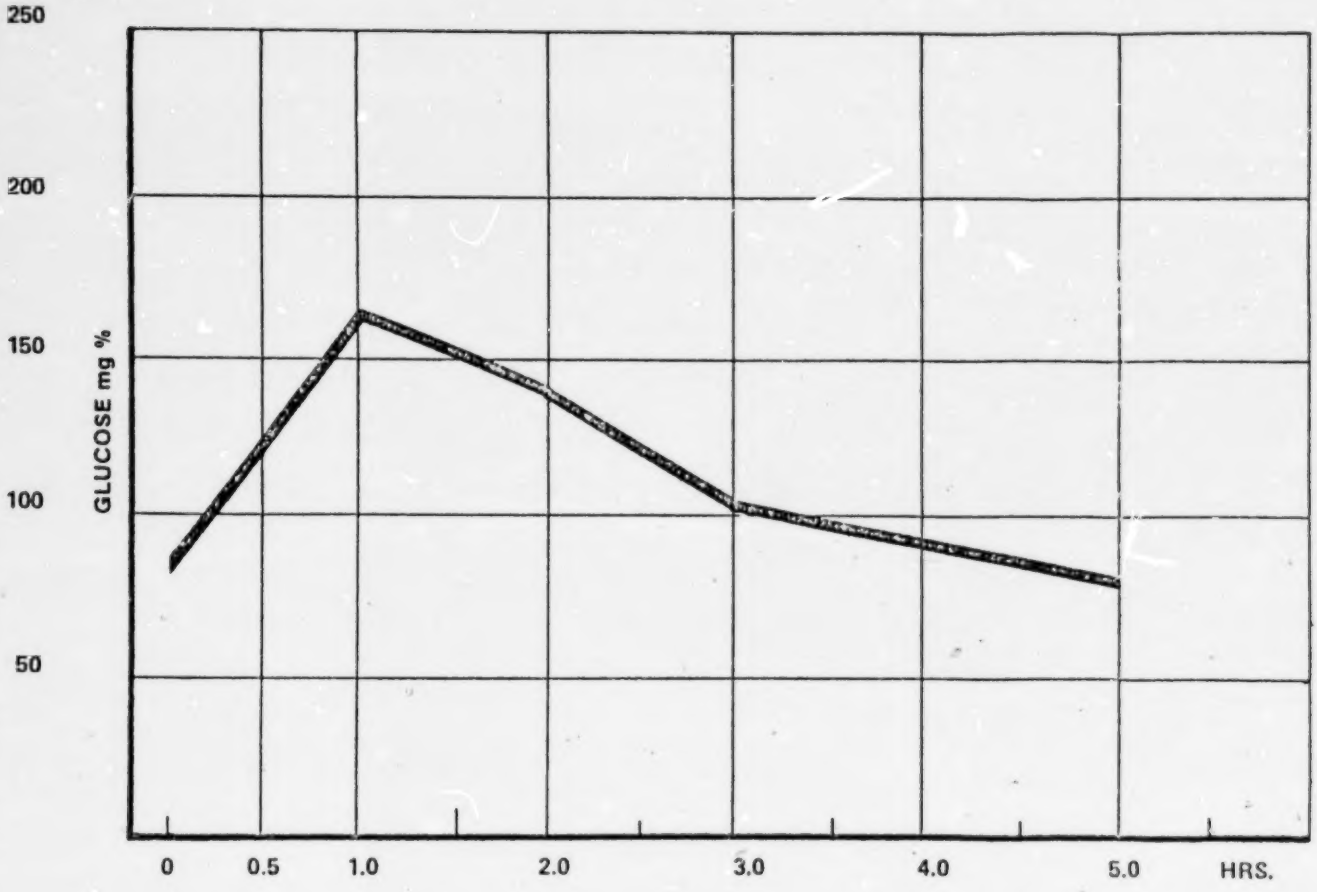
CASE: 117



RISE TIME 0.40 HRS.
PEAK VALUE 90
GRADIENT FROM PEAK TO 3 HOURS – 11.9
GRADIENT FROM PEAK TO 4 HOURS – 10.8
GRADIENT FROM PEAK TO 5 HOURS – 7.2

Fig. 2. Glucose Tolerance Test Curve Characterized by Low Flat Response.

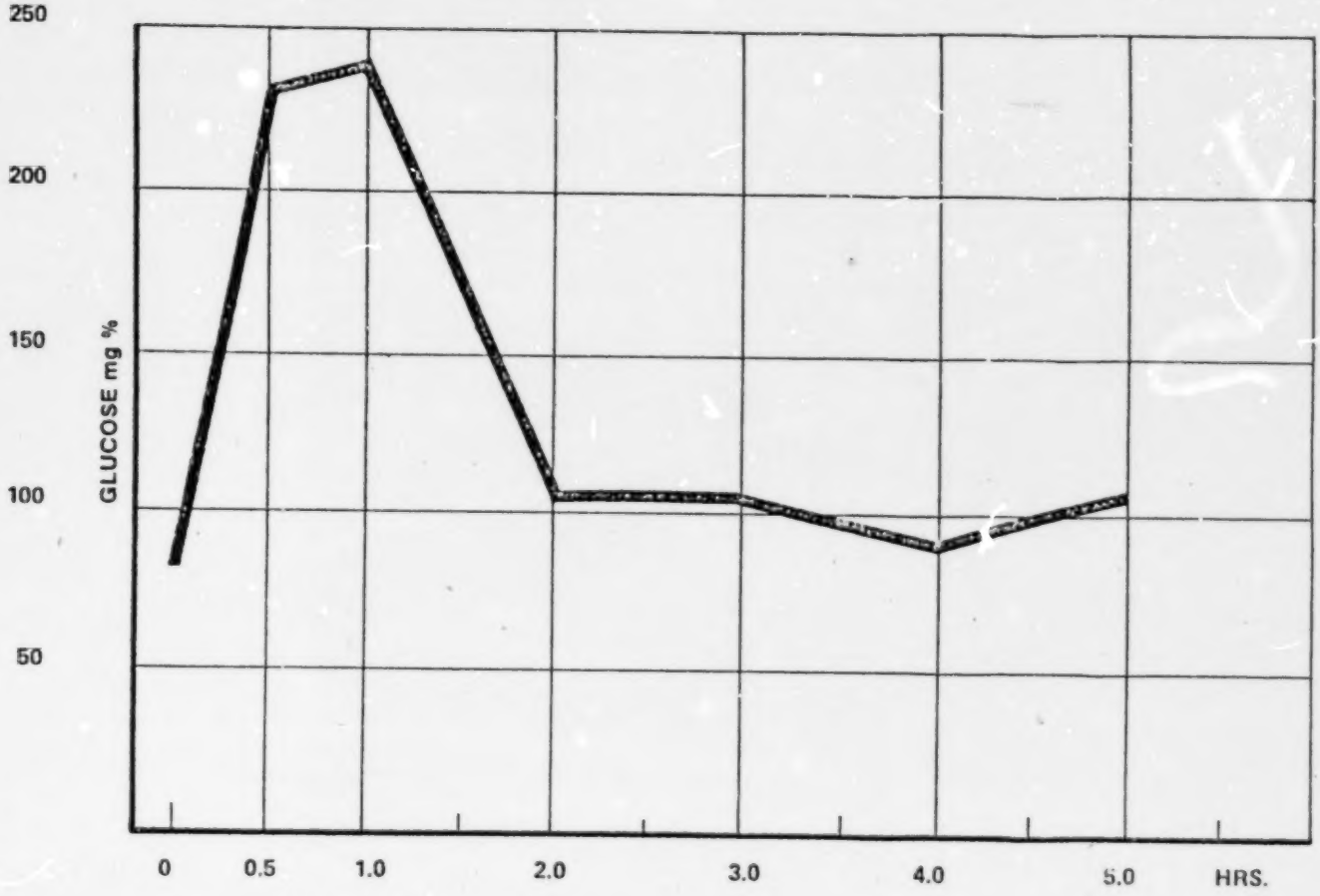
CASE: 207



RISE TIME 1.20 HRS.
PEAK VALUE 164
GRADIENT FROM PEAK TO 3 HOURS – 35.6
GRADIENT FROM PEAK TO 4 HOURS – 25.8
GRADIENT FROM PEAK TO 5 HOURS – 20.6

Fig. 3. Glucose Tolerance Curve with Excessive Peak and Slow Recovery.

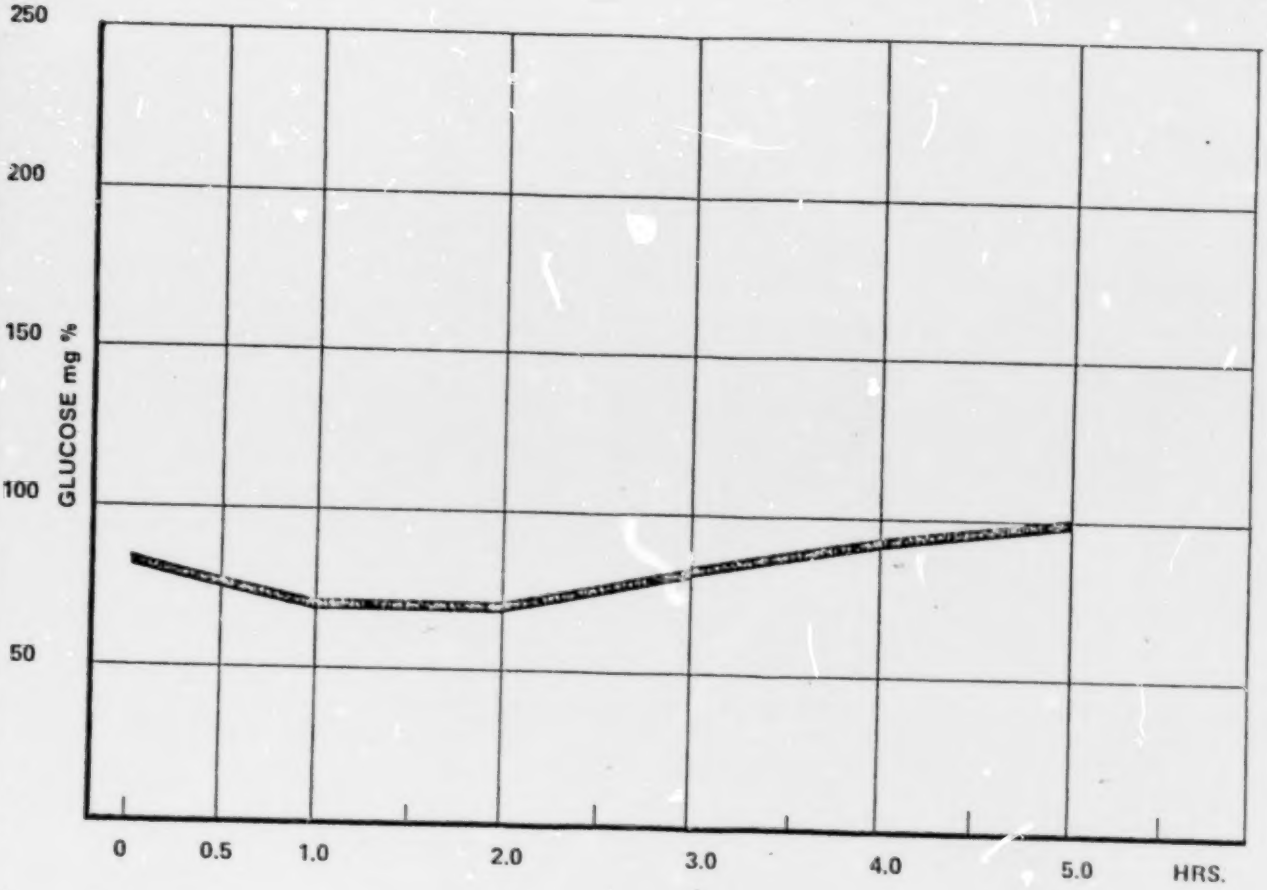
CASE: 239



RISE TIME 0.80 HRS.
PEAK VALUE 249
GRADIENT FROM PEAK TO 3 HOURS – 64.0
GRADIENT FROM PEAK TO 4 HOURS – 49.6

Fig. 4. Glucose Tolerance Test Curve with Excessive Peak and Rapid Decline.

CASE: 008



RISE TIME 5.00 HRS.
PEAK VALUE 104
GRADIENT FROM PEAK TO 3 HOURS – 9.5
GRADIENT FROM PEAK TO 4 HOURS – 14.0
GRADIENT FROM PEAK TO 5 HOURS – 31.3

Fig. 5. Glucose Tolerance Test Curve with "Half Moon" Shape.